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(21) International Application Number: PCT/GB97/00496 (22) International Filing Date: 24 February 1997 (24.02.97) (30) Priority Data: 9603945.8 24 February 1996 (24.02.96) GB (71) Applicant (for all designated States except US): THE UNIVERSITY COURT OF THE UNIVERSITY OF ST. ANDREWS [GB/GB]; College Gate, St. Andrews, Fife KY16 9AJ (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): GANI, David [GB/GB]; Bois-Fleuris, Brownhills Farm Steading, Crail Road, St. Andrews, Fife KY16 8PL (GB). AKHTAR, Mahmoud [GB/GB]; 4 Reid Gardens, St. Andrews, Fife KY16 8XR (GB). KROLL, Friedrich, Erich, Karl [DE/GB]; 19 Forrest Street, St. Andrews, Fife KY16 8HR (GB). SMITH, Colin, Forbes, MacDonald [GB/GB]; 26 Lamond Drive, St. Andrews, Fife KY16 8BE (GB). (74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: A MICROREACTOR (57) Abstract <p>A microreactor (20) for the synthesis of chemical compounds includes a container having a body section (21). Entry pores are provided to permit fluid to enter the container and a visual identification device is provided to enable visual identification of the microreactor (20).</p> <div data-bbox="808 1136 1373 1478"></div>		

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1 "A Microreactor"

2

3 The invention relates to a microreactor, and especially
4 a microreactor for synthesising chemical compounds.

5

6 Recent trends in the area of drug development,
7 biotechnology and chemical research have moved towards
8 producing large arrays of related molecules using
9 combinatorial (or permutational) synthesis. These new
10 techniques are potentially capable of yielding
11 libraries of millions of compounds which can be
12 screened, if a suitable assay is available, to identify
13 the required properties, for example biological
14 activity. The new methods have advantages because only
15 a relatively small number of chemical reaction vessels
16 need to be used, compared to the traditional methods in
17 which a single compound is sequentially processed
18 through various chemical transformations, usually one
19 reaction step at a time. The new method, combinatorial
20 synthesis, relies on the fact that under suitable
21 conditions several compounds can be converted into
22 several new products using a single reaction vessel.

23

24 The problems with combinatorial chemistry are manifold.
25 First, reaction chemistry needs to be irreversible,

1 such that each of the starting materials in the mixture
2 is converted to a new product. Second, at the present
3 time it is only feasible to perform combinatorial
4 chemistry for large libraries in the "solid-phase",
5 that is where the starting materials are covalently
6 bonded to a polymeric support, which is usually cross-
7 linked polystyrene. The advantages of solid-phase
8 synthesis are that the products do not need to be
9 purified by, for example, solvent extraction,
10 distillation, recrystallisation or chromatography but
11 rather are retained on the solid medium by washing away
12 the excess reagents and impurities. Thus, in solid-
13 phase synthesis (SPS) it is necessary to confine the
14 polymeric support so that it too is not washed away.

15
16 The third problem concerns the deconvolution of the
17 library which essentially requires identifying the
18 chemical structure of the molecule, within the mixture,
19 that shows the required biological activity or other
20 desired property. Clearly, when one is dealing with
21 mixtures of compounds, where the polymeric support for
22 one compound looks identical to another requires the
23 resynthesis of partial libraries of ever decreasing
24 size, coupled with assay in order to identify the
25 active material. This method of deconvolution is time
26 consuming and unnecessarily clumsy. Another way of
27 effecting deconvolution is to tag the polymeric support
28 with chemicals which can be used to decode the
29 synthetic chemical history of the particular particle
30 of polymeric support, independently to being able to
31 carry out an activity assay on the material attached to
32 the support. Such methods have been described in the
33 literature. Since typical particles of polymeric
34 support are referred to as "resin beads" and are
35 commercially available in the size 90-400 microns,
36 deconvolution by such methods is a fiddly job requiring

1 accurate and expensive instrumentation.

2

3 The fourth problem concerns checking the efficiency of
4 the chemical synthesis and, in essence, this is a
5 problem of scale. Individual beads possess, at most,
6 only a few nanomoles of material attached to them and
7 thus it is extremely difficult to check either the
8 efficiency of the synthesis or the purity of the
9 synthetic product. In highly sensitive biological
10 screening assays this can be a very serious problem as
11 the impurity could be responsible for a positive
12 result. The best way to overcome this last problem is
13 to perform syntheses on a larger scale such that some
14 material can be put aside for characterisation and
15 analysis. While this solution offers very many
16 advantages, the practice of larger scale combinatorial
17 syntheses requires the design and use of microreactors.
18 To date, only two reports of the use of microreactors
19 (or porous capsules) for solid-phase synthesis on a
20 polymeric support have been described, and the authors
21 supplied little information on the design of the
22 microreactors. The main purpose of the reports was to
23 describe the incorporation of an addressable microchip
24 into the microreactors which could be written to and
25 read using radio waves. This elegant idea does require
26 the microreactors to be of a size large enough to
27 contain the addressable chip, which in itself is not a
28 problem, but again demands the use of sophisticated and
29 expensive equipment for the identification of
30 individual compounds.

31

32 In accordance with a first aspect of the present
33 invention, a microreactor for synthesis of chemical
34 compounds comprises a container comprising a body
35 section; entry means to permit fluid to enter the
36 container; and a visual identification device to enable

1 visual identification of the microreactor.

2

3 The term "microreactor" as used herein means a
4 container comprising a material which is permeable to
5 fluids. The container may enclose a solid material or
6 particles on or with which reaction occurs, and the
7 container is impermeable to the solid material or
8 particles. Alternatively, the material of the
9 container itself may comprise a chemically
10 functionalised polymer on or with which reaction
11 occurs. This can be referred to as a "bonded"
12 microreactor.

13

14 The microreactor may further comprise a closure and the
15 body section may have an opening, the closure being
16 adapted to close the opening, and fluid being able to
17 enter the container through the entry means when the
18 opening is closed by the closure.

19

20 Alternatively, the body section may comprise a material
21 which comprises a polymeric support on or with which
22 reaction occurs. Typically, the polymeric support may
23 be chemically functionalised polystyrene and may be in
24 the form of a porus, frit or sintered material.

25

26 In accordance with a second aspect of the present
27 invention, a method of identifying a microreactor for
28 synthesis of chemical compounds comprises attaching a
29 visual identification device to the microreactor to
30 enable the microreactor to be visually identified.

31

32 An advantage of the invention is that it permits
33 deconvolution of a library of synthesised molecules by
34 visual identification of a microreactor.

35

36 Preferably, the visual identification device may

1 comprise a character and/or a colour. Typically, the
2 character may be an alphanumeric character.

3

4 Typically, the visual identification device may be
5 attached to the external surface of the container.
6 However, alternatively, the visual identification
7 device may be inserted into the container or may be
8 incorporated into the material of the container, which
9 may be the body section and/or the closure.

10

11 The closure may be removable or non-removable from the
12 opening.

13

14 Typically, each microreactor may comprise a number of
15 visual identification devices, which may be different
16 or identical.

17

18 The visual identification devices may be attached to
19 the microreactor prior to the microreactor being used
20 for synthesis of chemical compounds. Alternatively,
21 the visual identification devices may be attached as
22 appropriate before or after each stage in the synthesis
23 procedure, one at a time or several at a time.

24

25 The visual identification device may be of a size to be
26 visually identified by humans, or alternatively may be
27 identified by robotics or another type of machine.

28

29 Typically, a separate visual identification device is
30 provided for each chemical in which the microreactor is
31 immersed during synthesis.

32

33 In one example of the invention, the body section may
34 have two openings and two removable closures, one
35 closure for each opening. Typically, in this example
36 of the invention, the body section may be tubular with

1 the openings provided at each end of the tubular body
2 section.

3

4 In a second example of the invention, there may be just
5 one opening in the body section, which may be
6 cylindrical in form.

7

8 In the case of bonded microreactors which themselves
9 consist of chemically functionalised frit glass or frit
10 or foamed polymer, there do not need to be openings for
11 loading and unloading of resin, as the chemically
12 reactive groups would be retained within the bonded
13 matrix itself.

14

15 Where the visual identification device is attached to
16 the outer surface of the container, the device may
17 comprise a ring shaped member which is fitted over the
18 body section and visual identification may be provided
19 by a colour of the member and/or by characters on the
20 surface of the member.

21

22 Alternatively, the visual identification device may be
23 inserted into holes or apertures in a side wall of the
24 container. For example, the visual identification
25 device may comprise a peg or bead which fits into and
26 is held in the hole or aperture.

27

28 Preferably, the entry means is provided by apertures in
29 the side walls of the container. The side walls may
30 comprise frit material, a perforated polymer material
31 or a mesh. It is possible that a combination of these
32 materials could be used. Examples of suitable frit
33 materials are frit glass, frit polyethylene, frit
34 polypropylene and frit polytetrafluoroethylene (PTFE).

35

36 The closure may be attached to the body section by

1 being a push fit into the opening, by being threadedly
2 connected to the body section or attached by an
3 adhesive.

4
5 Typically, for biological applications, the
6 microreactors may have a length of approximately 7-
7 10mm, and internal width of 3.5-7mm and an outside
8 width of 4-10mm. Typically, the microreactors are for
9 use with standard commercially available polymer beads
10 of 90-400 microns for solid support in the solid phase
11 synthesis.

12
13 However, these dimensions should not be considered as
14 being limiting and larger microreactors or smaller
15 microreactors may be constructed for other
16 applications. For example larger microreactors may be
17 constructed and used for non-biological applications.

18
19 Typically, the microreactor and the visual
20 identification device are composed of cheap inert
21 material and the selection of the materials is dictated
22 by the intended chemistry, ie only compatible materials
23 are used, eg glass is not used with aqueous
24 hydrofluoric acid and non-resistant polymers are not
25 used with organic solvents.

26
27 Examples of a microreactor in accordance with the
28 invention will now be described with reference to the
29 accompanying drawings, in which:-

30
31 Fig. 1 is a cross sectional view through a first
32 example of a microreactor;

33 Fig. 2 is a cross sectional view through a second
34 example of a microreactor;

35 Fig. 3 is a perspective view of a third example of
36 a microreactor;

1 Fig. 4 is a plan view of the microreactor shown in
2 Fig. 3;
3 Fig. 5 is a front view of the microreactor shown
4 in Fig. 3;
5 Fig. 6 is a back view of the microreactor shown in
6 Fig. 3;
7 Fig. 7 is an exploded side view of a fourth
8 example of a microreactor;
9 Fig. 8 is a side view of the microreactor of Fig.
10 7 assembled; and
11 Fig. 9 is a flow diagram illustrating how twenty-
12 seven microreactors may be used to synthesise
13 twenty-seven compounds from three suitably
14 functionalised starting compounds.

15
16 Fig. 1 shows a first example of a microreactor 1 which
17 comprises a polymer tube having 70 micron perforations
18 in the wall of the tube 2. At each end of the tube 2
19 is an end cap 3. The material from which the tube 2
20 and end caps 3 are manufactured is inert with the
21 compounds into which the microreactor 1 is to be
22 immersed. Located within the microreactor 1 are a
23 number of polymer beads 4 for solid support in solid
24 phase synthesis. The polymer beads have a diameter
25 which is greater than 70 microns.

26
27 A second example of a microreactor 5 is shown in Fig.
28 2. The microreactor 5 comprises a container body
29 section 6 having an open end 7 which is closed by a
30 removable lid 8. The container body section 6 and the
31 removable lid 8 are both manufactured from frit glass
32 and the frit glass is chosen to be inert with the
33 compounds in which the microreactor 5 is to be
34 immersed. However, any other suitable frit material
35 may be used. The microreactor 5 also contains a number
36 of polymer beads for solid support in solid phase

1 synthesis.

2

3 Figs. 3 to 6 show a third example of a microreactor 20
4 which is manufactured from a frit material. This may
5 be frit glass, frit polyethylene, frit
6 polytetrafluoroethylene or any other suitable frit
7 material. A "suitable frit material" is any frit
8 material which is inert with the chemicals into which
9 the microreactor 20 is to be immersed.

10

11 The microreactor 20 consists of a cylindrical body
12 section 21 which has a hole 22 drilled into the curved
13 surface of the cylindrical body section 21. Hole 22
14 has polymer beads inserted into it before the hole 22
15 is plugged by a plug 23. Around the curved surface of
16 the body section 21 a number of small holes 24 are
17 drilled. These holes permit small coloured pegs to be
18 attached to the microreactor 20 by being pushed into
19 the holes 24.

20

21 After the hole 22 has been plugged by the plug 23, the
22 plugged hole 22 forms a reaction chamber into which
23 chemical fluids may enter through the holes in the frit
24 material from which the body section 21 is formed. The
25 plug 23 may be any suitable inert material, such as an
26 inert polymer.

27

28 As an alternative to the microreactor 20, the
29 microreactor could be manufactured from porous or frit
30 perfluoroalkyl sulphonic acid resin, such as Nafion
31 (trade mark) manufactured by Du Pont, so that the
32 material of the microreactor itself forms the polymeric
33 support. In addition, or alternatively, other
34 chemically functionalised sintered, frit or porous
35 polymers or composites could be used to form the
36 microreactor.

1 In this example, the microreactor would not have the
2 reaction chamber 22 or the closure 23 and would be a
3 body of material porous or frit material. However, the
4 holes 24 for the coloured pegs would still be present.
5 The reactions then take place on or with the material
6 of the microreactor itself.

7
8 Figs. 7 and 8 show a fourth example of a microreactor
9 30. Fig. 7 is an exploded side view of the
10 microreactor 30 showing the components of the
11 microreactor 30. The microreactor 30 has a tubular
12 glass body 31 which has an external screw thread
13 formation 32. The body 31 is hollow and two sealing
14 rings 33 and a frit glass end closure 34 are secured to
15 each end of the glass body 31 by an end cap 35. The
16 end caps 35 are internally threaded so that they screw
17 onto the thread 32 on the body 31.

18
19 If the end closures 34 are of a frit material, such as
20 a plastic, it would not be necessary to use the sealing
21 rings 33.

22
23 In use, one end cap 35, end closure 34 and sealing
24 rings 33 are secured to one end of the body 31. The
25 polymer beads may then be placed in the body 31 through
26 the other open end. The open end is then closed using
27 the other end cap 35, end closure 34 and sealing rings
28 33.

29
30 The visual identification devices for the microreactor
31 30 may be moulded into the end caps 35, which may be
32 moulded from a plastics material. In addition, it is
33 possible that the end caps 35 and/or body 31 may be
34 individually colour coded.

35
36 In this example the body 31 is solid glass and not frit

1 glass.

2

3 Fig. 8 shows the assembled microreactor 30. In the
4 microreactor 30, the fluids enter the microreactor
5 through the end closures 34 which are of a frit
6 material, and therefore permeable to fluids but not to
7 the polymer beads placed inside the microreactor 30.

8

9 Both frit glass tubes and rectangular chambers and
10 perforated polymer tubes and meshes with appropriate
11 lids were used as microreactors in the synthesis of
12 small peptide libraries. Standard commercially
13 available polymer beads 4 of 90-400 microns were used
14 for the solid support in the solid phase synthesis
15 (SPS). Essentially, the dimensions of the
16 microreactors range from a length of 7-10mm, with an
17 internal diameter of 3.5-7mm, and an outside diameter
18 of 4-10mm, depending on the material. The walls of
19 frit glass tube need to be thicker to provide
20 mechanical strength. The lids 3, 8 of the
21 microreactors 1, 5 and the plug 23 of the microreactor
22 20 are resistant polymer or frit glass and can be
23 colour coded as part of the visually addressable
24 system. The microreactors 1, 5, 20 themselves can also
25 be colour coded or marked with the appropriate alpha-
26 numeric or icon, or with multiple visual
27 identifications. Larger microreactors can be
28 constructed for non-biological applications using the
29 same material and protocols outlined here.

30

31 The microreactors used were pre-labelled, that is the
32 colours and alpha-numerics were already associated with
33 each of the microreactors such that the chemical
34 synthesis was programmed by the visual identification
35 marks. In principle, this method offers no advantages
36 or disadvantages in identification compared with

1 tagging the microreactors after each cycle of the
2 synthesis. However, pre-labelled microreactors could
3 be used in programmed robotic synthesis, where the
4 machine or human readable identification is used to
5 determine which vessel the microreactor is placed into
6 for the next step. Another advantage is that
7 microreactors could be manufactured and supplied in a
8 coded form for the user to predetermine what each
9 element of the code will mean in the synthesis of the
10 chemical libraries. This also saves the user from
11 needing to tag the microreactor after each step.
12 Moreover, precision machine labelled microreactors have
13 the potential to be smaller than those described above
14 where for human visualisation, as opposed to robotic
15 identification, the microreactor is read using a
16 magnifying glass, typically of the type used by
17 electronics engineers for identifying resistors and
18 chips etc.

19
20 The limit of the number of sets of colours,
21 alphanumerics, etc that can be read easily on the
22 microreactors described above is six, without the aid
23 of a magnifying glass. This number could be increased
24 to twelve by precision manufacture of the microreactors
25 for visual identification using a magnifying glass.
26 However, in practise, twelve represents the number of
27 actual synthetic steps (not counting chemical
28 activation and protection and deprotection steps which
29 support the synthetic chemistry) and twelve is probably
30 beyond the need of any potential application other than
31 bioactive peptide synthesis. The structural
32 (molecular) diversity is limited by the visualisation
33 method. For example, there are ten easily
34 distinguishable colours and if all ten are used for
35 each of six syntheses steps there are 10^6 individually
36 addressable microreactors. For easily distinguishable

1 letters (of which there are 24, not counting Greek
2 letters) there are $24^6 = 191$ million addressable
3 microreactors. For a two digit numeric labelling
4 strategy there are 9.4148×10^{11} individually
5 addressable microreactors. In practise these numbers
6 are much larger than those required and typically
7 libraries of microreactors would be 9-10,000 in size.
8 Where the overall volume of each microreactor is 0.25-
9 0.75 cm^3 . a library of 10,000 compounds could be
10 prepared easily in conventional laboratory scale
11 equipment. Note that for a diversity factor of 10, ten
12 separate reactions on 1000 compounds in 1000
13 microreactors would be performed in the last step to
14 give a library of 10,000 compounds. 1000 microreactors
15 would fit inside a vessel of $1000\text{-}2000 \text{ cm}^3$ and leave
16 plenty of room for the solvent and
17 mixing/heating/cooling and sensing equipment. Typical
18 large scale laboratory equipment has a maximum capacity
19 of $10,000 \text{ cm}^3$. Vessels larger than this require special
20 facilities.

21
22 In a typical but non-restrictive protocol for peptide
23 library or other compound library synthesis, a small
24 amount of pre-swollen commercially available resin for
25 solid phase peptide synthesis is added to the pre-
26 labelled microreactor as a slurry in dimethylformamide
27 such that the microreactor is half-full or less. A
28 small glass bead or stirring magnet may be added to
29 ensure thorough mixing. The microreactor, and any
30 others which are to be processed, are placed in the
31 main reaction vessel and are drowned in a solution of
32 solvent eg dimethylformamide containing the appropriate
33 reagents for either synthesis or deprotection in the
34 usual way. The microreactors are physically agitated to
35 ensure that each resin bead is exposed to the reagent
36 solution. The microreactors are then transferred to

1 new appropriate reaction vessels, together with other
2 microreactors, as dictated by the visually addressable
3 labels for further cycles of deprotection of synthesis.
4 The entire process is repeated until the synthesis and
5 deprotection is complete. The library of labelled
6 microreactors is now ready for solid phase assay (on
7 the polymer bead) where individual beads are removed to
8 prepare a library or sub-library of beads of known
9 composition. If solution phase assays are to be
10 performed, the compounds are obtained by un-linking the
11 polymer resin support. This can be performed either on
12 the entire contents of any or all of the individual
13 microreactors, or on just a portion of the contents.
14 Unlinking is performed in the usual way. In our
15 experiments we used Fmoc peptide chemistry and removed
16 the compounds from the resin using trifluoroacetic
17 acid. The purity and structure of the library members
18 was assessed by nmr spectroscopy. Note that for
19 unlabelled microreactors, one identification tag (eg a
20 thin inert polymer ring or peg of a given colour or
21 marked with a specific alphanumeric or icon) would be
22 added either prior to, or, immediately after placement
23 in a reaction vessel for every synthesis.

24
25 In the case of bonded microreactors composed of porous
26 functionalised polymer, for example, perfluoroalkyl
27 sulphonic acid or carboxylic acid resins such as Nafion
28 or those manufactured by Asahi or Dow, the acid groups
29 would be activated to load appropriate nucleophilic
30 linker groups, for example, 3-aminobenzyl alcohol to
31 give a chemical reaction surface similar to that for
32 commercially available resins.

33
34 To illustrate how the visually interrogatable coding
35 would work in the construction of a combinatorial
36 library using permutational organic synthesis in

1 addressable microreactors (POSAM), consider a library
2 10 of twenty-seven compounds made up from three
3 structural moieties called A, B and C (see Fig. 9).
4 Twenty-seven microreactors 11 are provided. In the
5 first cycle of the reaction nine microreactors 11 are
6 reacted with compound A, nine with B and nine with C,
7 in separate vessels, to load the polymeric beads in the
8 microreactors 11 with compounds A, B and C
9 respectively. The microreactors 11 from each of the
10 three vessels are then tagged with a visual
11 identification mark such that the microreactors 11
12 loaded with A, B and C can be discriminated.

13
14 In the second cycle of synthesis, three of the
15 microreactors 11 containing compound A, three
16 containing B and three containing C are then reacted
17 with compound A. When the reaction is complete the
18 microreactors 11 are labelled with a further visually
19 identifiable tag. Nine further microreactors 11
20 containing A, B and C (three of each) are then reacted
21 with compound B and then tagged and the remaining nine
22 microreactors 11 containing A, B and C are then reacted
23 with compound C and then tagged. Thus there are now
24 three sets 12 of nine differentially labelled
25 microreactors containing the compounds AA, BA, CA, AB,
26 BB, CB, AC, BC and CC (see Fig. 9).

27
28 In a third cycle, one set of the nine compounds is
29 reacted with compound A, and then tagged and a further
30 set of nine reacted with compound B, and then
31 differentially tagged and finally, the last set of nine
32 compounds is reacted with compound C and then tagged.
33 This gives a final library of twenty-seven different
34 compounds attached to the polymer support inside the
35 twenty-seven microreactors 11 which are all
36 individually distinguishable merely by looking at them.

1 The visual identification of microreactors also ensures
2 that no mistakes are made during various cycles of
3 library synthesis and avoids the statistical problems
4 generated in the split and mix strategy that is used
5 when dealing directly with the indistinguishable
6 polymeric beads. If the synthetic efficiency of the
7 chemical process needs to be interrogated, it is either
8 possible to open up a microreactor and remove some of
9 the material for analysis or to include extra identical
10 microreactors visually tagged in the appropriate manner
11 which are removed during the synthetic procedure,
12 specifically for analysis.

13
14 The protocols described are suitable for a wide range
15 of chemistries with reactors of a small size, as
16 described here, up to quite large sizes eg 20 cm³ per
17 reactor. In industry and with special vessels even
18 larger reactors could be used. Clearly, the larger the
19 reactor the more easily it can be visually addressed.
20 This patent should cover any confined solid support
21 chemical reactor used to generate libraries of
22 compounds greater than four members in two or more
23 synthetic cycles either sequentially or simultaneously
24 in larger reaction vessels where reactors are addressed
25 by any visual interrogation system employing colour,
26 alphabetic, numeric bar-coding or icon based system.

1 CLAIMS

2

3 1. A microreactor for synthesis of chemical compounds
4 comprising a container comprising a body section; entry
5 means to permit fluid to enter the container; and a
6 visual identification device to enable visual
7 identification of the microreactor.

8

9 2. A microreactor according to claim 1, wherein the
10 body section comprises a body of material, the material
11 comprising a polymeric support on or with which
12 reaction occurs.

13

14 3. Apparatus according to claim 1, wherein the body
15 section has an opening and the container further
16 comprises a closure adapted to close the opening; and
17 the entry means permits fluid to enter the container
18 when the opening is closed by the closure.

19

20 4. A microreactor according to any of the preceding
21 claims, wherein the visual identification device
22 comprises a character and/or a colour.

23

24 5. A microreactor according to claim 4, wherein the
25 character is an alphanumeric character.

26

27 6. A microreactor according to any of the preceding
28 claims, wherein the visual identification device is
29 attached to the external surface of the container.

30

31 7. A microreactor according to any of the preceding
32 claims, wherein the visual identification device is
33 incorporated into the material of the container.

34

35 8. A microreactor according to any of the preceding
36 claims, wherein a microreactor comprises a number of

1 visual identification devices.

2

3 9. A microreactor according to any of the preceding
4 claims, wherein the entry means is provided by
5 apertures in the side walls of the container.

6

7 10. A microreactor according to claim 9, wherein the
8 side walls of the container are porous.

9

10 11. A microreactor according to any of the preceding
11 claims, wherein the visual identification device is
12 inserted into holes or apertures in a side wall of the
13 container to attach the visual identification device to
14 the container.

15

16 12. A method of identifying a microreactor for
17 synthesis of chemical compounds comprises attaching a
18 visual identification device to the microreactor to
19 enable the microreactor to be visually identified.

20

21 13. A method according to claim 12, wherein the visual
22 identification devices are attached to the microreactor
23 prior to the microreactor being used for synthesis of
24 chemical compounds.

25

26 14. A method according to claim 12, wherein the visual
27 identification devices are attached where appropriate
28 before or after each stage in the synthesis procedure.

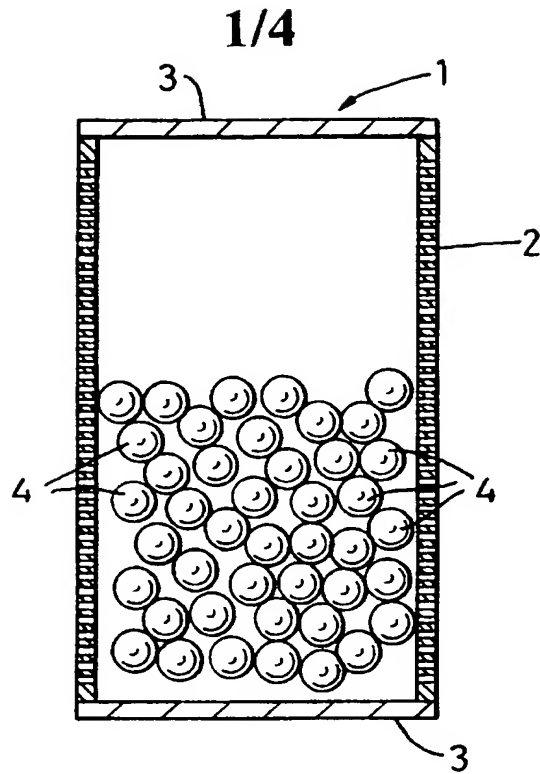


Fig. 1

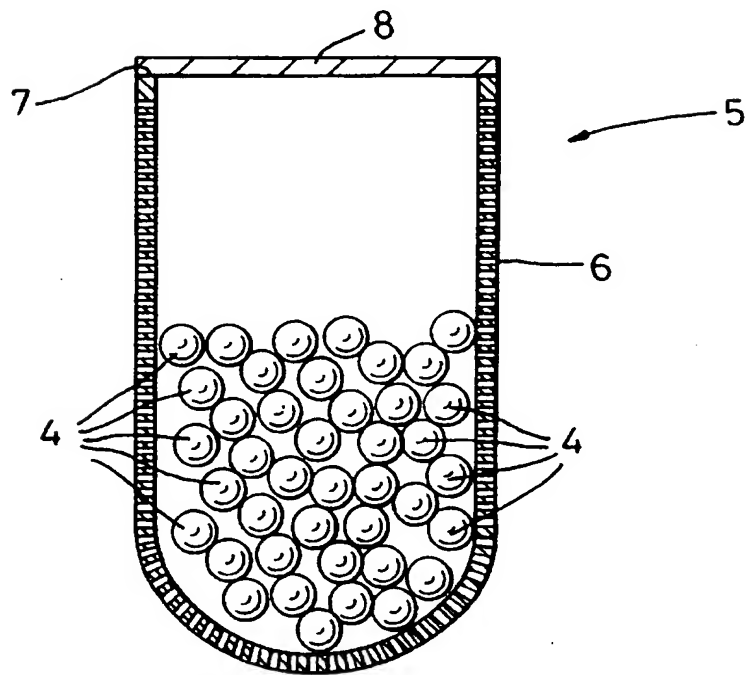


Fig. 2

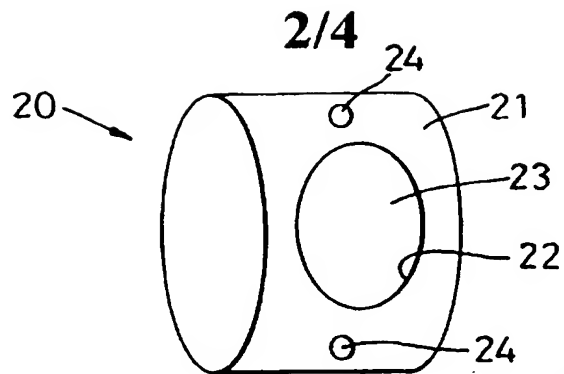


Fig. 3

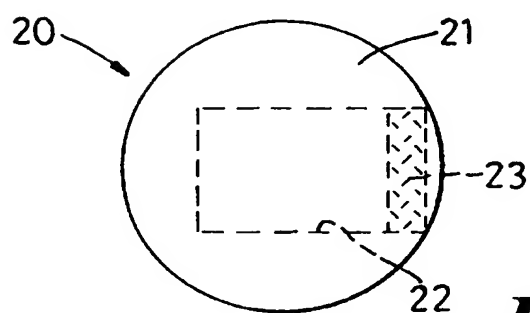


Fig. 4

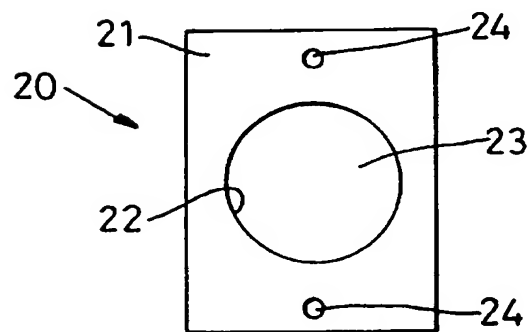


Fig. 5

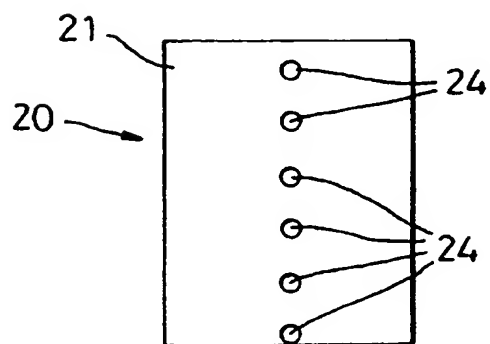


Fig. 6

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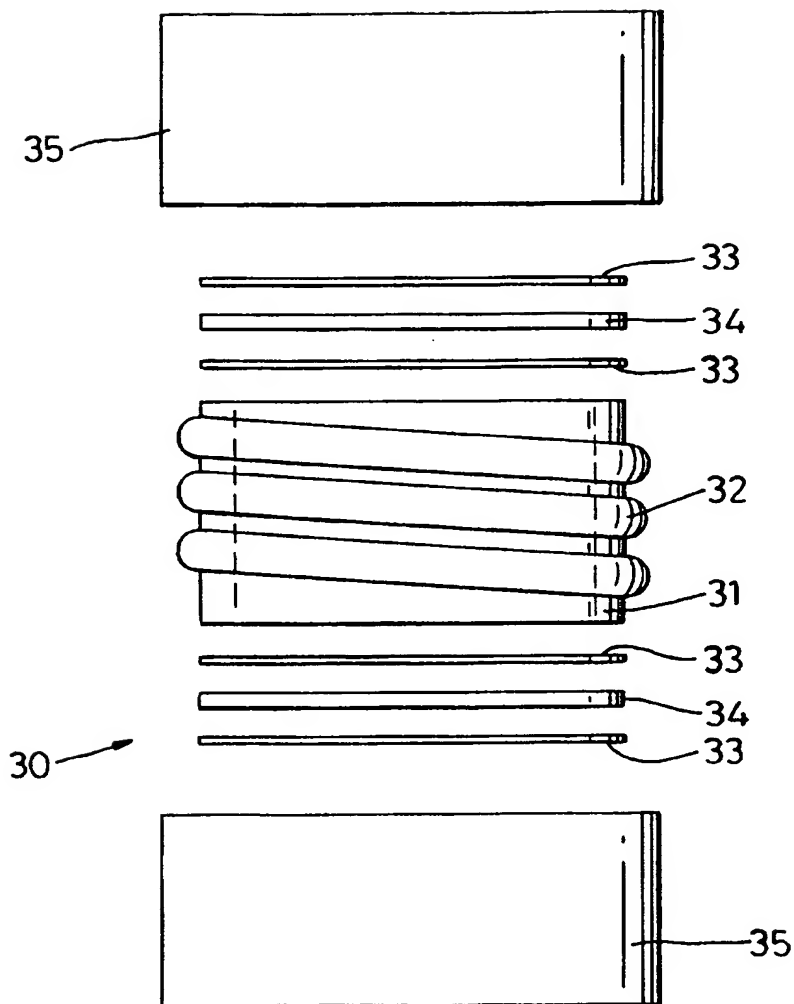


Fig. 7

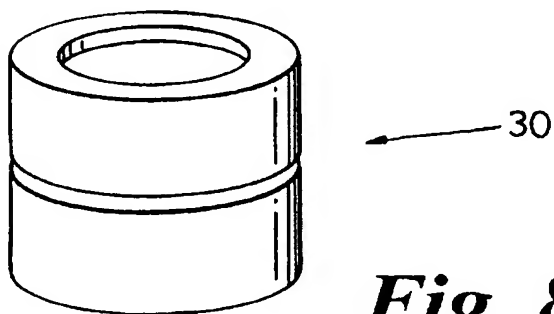
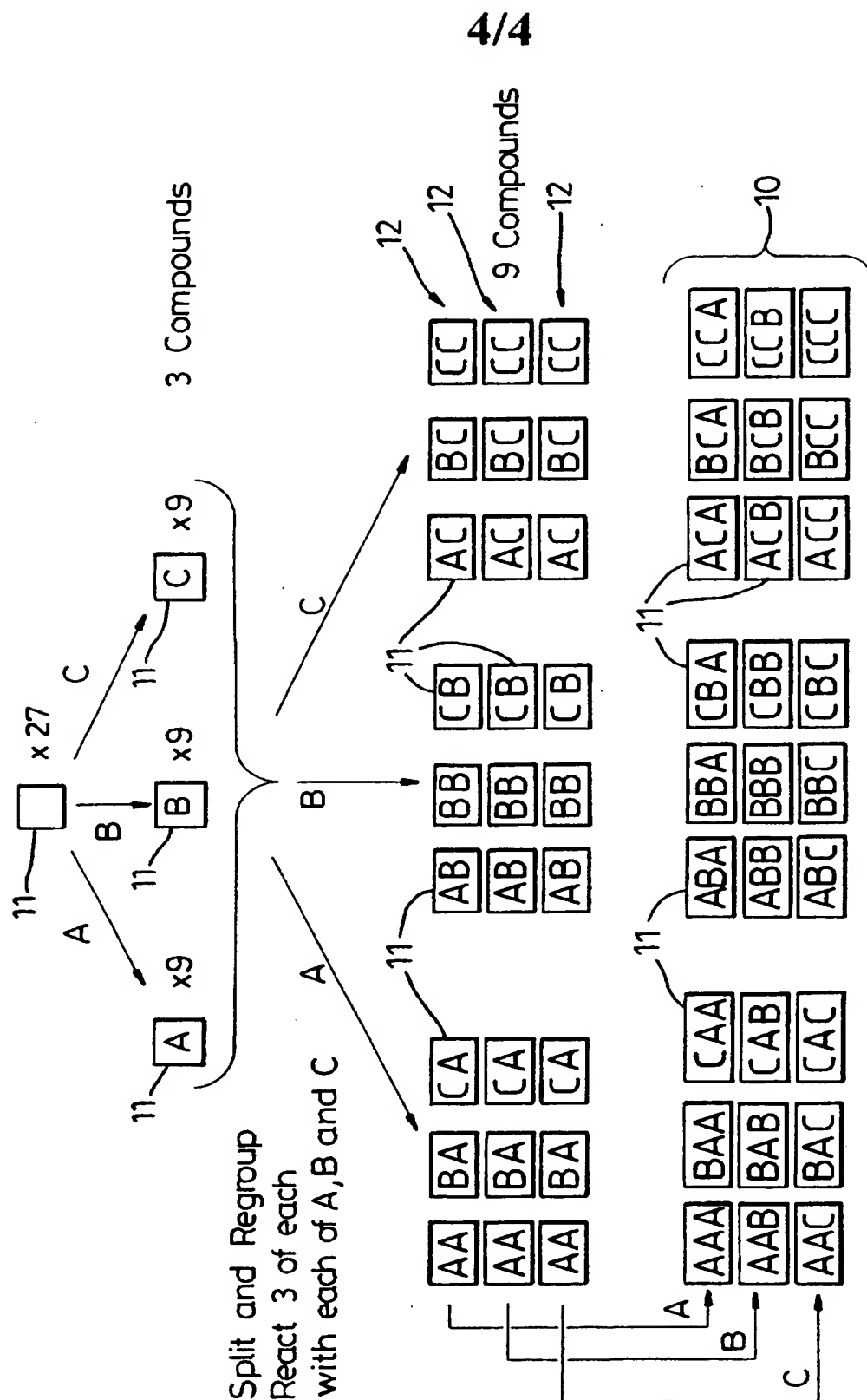


Fig. 8



INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 97/00496

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 B01J19/00 C07K1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12M B01J C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	EP 0 156 588 A (APPLIED BIOSYSTEMS) 2 October 1985	1-10, 12-14
Y	see page 40 - page 42; claims 1-6; figures 1-5	1-11
Y	--- EP 0 196 174 A (SCRIPPS CLINIC RES) 1 October 1986 see page 21; figure 5B	11
Y	--- FR 2 526 169 A (MOCHIDA PHARM CO LTD) 4 November 1983 see claims; figures ---	1,2,4-8
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

13 June 1997

Date of mailing of the international search report

01.07.97

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Coucke, A

INTERNATIONAL SEARCH REPORT

Internal Application No

PCT/GB 97/00496

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Information on patent family members

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